

Listing of Claims:

1. (Previously Presented) A bone material and hard tissue replacement material comprising, in combination, a mixture of:

a calcium phosphate compound capable of forming a chemically compatible *in vivo* bone or hard tissue replacement composition; and

at least first and second macropore forming materials, said first and second macropore forming materials each have a dissolution rate *in vivo*, at least one of said macropore forming materials characterized by increasing the flexural strength of said mixture *in vivo* by at least about 50%.

2. (Original.) The mixture of Claim 1 wherein the macropore forming materials are selected from the group consisting of fibers, rods, mesh, particles, crystals and combinations thereof.

3. (Original.) The mixture of Claim 1 further including stable filler materials not generally soluble *in vivo*.

4. (Original.) The mixture of Claim 1 wherein the macropore forming materials include a mesh which dissolves to provide a cross-connected macroporous structure in a matrix of the hardened calcium phosphate compound.

5. (Original.) The mixture of Claim 1 wherein the mixture comprising the composite is comprised, at least in part, of separate, discrete regions of mixtures of the calcium phosphate compound and one of said macropore forming materials.

6. (Original.) The mixture of Claim 5 wherein the separate regions are adjacent layers.

7. (Original.) The composite of Claim 5 wherein the separate regions include an outside region and an adjacent inside region and wherein the dissolution rate of the outside region macropore forming material exceeds the dissolution rate of the inside region macropore forming material.

8. (Original.) The mixture of Claim 5 wherein at least two separate regions include macropore forming materials having distinct geometric configurations.

9. (Original.) The mixture of Claim 5 wherein at least two separate regions include a combination of distinct macropore forming materials.

10. (Original.) The mixture of Claim 5 wherein the calcium phosphate compound is distinct in two distinct regions.

11. (Withdrawn.) The mixture of Claim 1 *in vivo*.

12. (Original.) The mixture of Claim 1 in the form of a bone replacement pre-form.

13. (Original.) The mixture of Claim 1 wherein the mixture is non-rigid.

14. (Original.) The mixture of Claim 1 wherein the mixture is elastomeric.

15. (Original.) The mixture of Claim 1 further including an additive selected from the group consisting of viscosity adjustment compounds, biologic compounds, pharmacologic

compounds, marker compounds, sterilizing agents, accelerator compounds, at least one insoluble stable filler material, and combinations thereof.

16. (Original.) The mixture of Claim 1 wherein the calcium phosphate compound comprises a mixture of tetracalcium phosphate and dicalcium phosphate anhydrous.

17. (Original.) The mixture of Claim 1 wherein the calcium phosphate compound forms a hydroxyapatite-containing solid when exposed to water.

18. (Original.) The mixture of Claim 1 wherein at least one of the macropore forming materials is selected from the group consisting of mannitol, sodium phosphate, sodium bicarbonate, and mixtures thereof.

19. (Previously Presented.) The mixture of Claim 1 wherein at least one of the macropore forming materials comprises a gradient of dissolution rates in the mixture.

20. (Original.) The mixture of Claim 1 wherein the macropore forming materials comprise at least two separate, homogeneous sections in the mixture.

21. (Original.) The mixture of Claim 1 wherein the macropore forming materials comprise at least two separate sections, each section having a distinct gradient dissolution rate.

22. (Original.) The mixture of Claim 1 wherein the macropore forming materials comprise at least two separate sections in said mixture, one of said sections comprising a homogeneous dissolution rate section and another of said sections having a gradient dissolution rate.

23. (Previously Presented.) The mixture of Claim 1 wherein at least one of said macropore forming materials are selected from the group of fast dissolution rate materials consisting of glass, ceramics, polymers and combinations thereof.

24. (Currently Amended.) A method of bone replacement comprising the steps of:

- (a) mixing the composition of any of claim [~~1-24~~] 1-11 and 12-23; and
- (b) placing said mixture *in vivo*.

25. (Currently Amended.) A method of hard tissue replacement comprising the steps of:

- (a) mixing the composition of any of claims [~~1-24~~] 1-11 and 12-23; and
- (b) placing said mixture *in vivo*.

26. (Previously Presented.) The mixture of claim 1 wherein said first macropore forming material is selected from the group consisting of fast dissolution rate materials, medium dissolution rate materials, slow dissolution rate materials, stable materials, and mixtures thereof and said second macropore forming material is selected from the group consisting of fast dissolution rate materials, medium dissolution rate materials, slow dissolution rate materials, stable materials and combinations thereof.

27. (Original.) The mixture of claim 1 further including an additional additive selected from the group consisting of elastomeric agents, fast hardening agents, gelling agents, stable filler materials and combinations thereof.

28. (Original.) The mixture of claim 27 wherein the elastomeric agent is selected from the group consisting of chitosan, chitosan derivatives and combinations thereof.

29. (Original.) The mixture of claim 27 wherein the fast hardening agent is sodium phosphate solution.

30. (Original.) The mixture of claim 27 wherein the gelling agent is selected from the group consisting of hydroxypropyl methylcellulose, carboxyl methylcellulose, starch, proteoglycans, glycoproteins and combinations thereof.

31. (Original.) The mixture of claim 27 wherein the insoluble agent is selected from the group consisting of metal, carbon and combinations thereof.

32. (Original.) The mixture of claim 1 wherein said calcium phosphate compound is selected from the group consisting of tetracalcium phosphate and dicalcium phosphate anhydrous cements, alpha-tricalcium phosphate cements, beta-tricalcium phosphate cements, dicalcium phosphate anhydrous cements, amorphous calcium phosphate cements and combinations thereof.

33. (Previously Presented.) The mixture of claim 1 wherein at least one of said macropore forming materials is characterized by at least a medium dissolution rate *in vivo*.

34. (Previously Presented.) The mixture of claim 1 wherein the macropore forming materials include meshes or fibers which dissolve to provide a cross-connected macroporous structure in a matrix of the hardened calcium phosphate compound, said cross-connected macroporous structure having interconnected cylindrical shapes from the dissolution of meshes or fibers to improve the tissue ingrowth process into the macroporous implant *in vivo*.

35. (Previously Presented.) The mixture of claim 1 wherein said macropore forming materials are in combination characterized by increasing the flexural strength of said mixture.

36. (Previously Presented.) The mixture of claim 1 wherein said macropore forming materials are in combination characterized by a dissolution rate greater than about one week *in vivo*.

37. (Previously Presented.) The mixture of claim 1 wherein one of said macropore forming materials has a fast dissolution rate and another macropore forming material has a medium or slow dissolution rate.

38. (Previously Presented.) A bone material and hard tissue replacement material comprising, in combination, a mixture of:

a calcium phosphate compound capable of forming a chemically compatible *in vivo* bone or hard tissue replacement composition; and

at least first and second macropore forming materials, said first and second macropore forming materials each having a dissolution rate *in vivo*, said materials in combination characterized by a dissolution rate greater than about one week *in vivo*.

39. (Previously Presented.) The bone material and hard tissue replacement material of claim 38 wherein said combination of first and second macropore forming materials is characterized by increasing the flexural strength of said mixture *in vivo* by at least about 50%.

40. (Previously Presented.) The mixture of claim 1 wherein the first macropore forming material comprises, at least in part, said compound.

41. (Previously Presented.) The bone material and hard tissue replacement material of claim 38 wherein said combination of first and second macropore forming materials is characterized by increasing the toughness of said combination by at least about two orders of magnitude relative to a control comprising said compound.

42. (Previously Presented.) The mixture of claim 1 wherein the toughness of said mixture is increased by at least about two orders of magnitude relative to a control comprising said compound.